Stent Placement in Acute Cerebral Artery Occlusion
Use of a Self-Expandable Intracranial Stent for Acute Stroke Treatment

Caspar Brekenfeld, MD; Gerhard Schroth, MD; Heinrich P. Mattle, MD; Do-Dai Do, MD; Luca Remonda, MD; Pasquale Mordasini, MD; Marcel Arnold, MD; Krassen Nedeltchev, MD; Niklaus Meier, MD; Jan Gralla, MD

Background and Purpose—Stent placement has been applied in small case series as a rescue therapy in combination with different thrombolytic agents, percutaneous balloon angioplasty (PTA), and mechanical thromboembolectomy (MT) in acute stroke treatment. These studies report a considerable mortality and a high rate of intracranial hemorrhages when balloon-mounted stents were used. This study was performed to evaluate feasibility, efficacy, and safety of intracranial artery recanalization for acute ischemic stroke using a self-expandable stent.

Methods—All patients treated with an intracranial stent for acute cerebral artery occlusion were included. Treatment comprised intraarterial thrombolysis, thromboaspiration, MT, PTA, and stent placement. Recanalization result was assessed by follow-up angiography immediately after stent placement. Complications related to the procedure and outcome at 3 months were assessed.

Results—Twelve patients (median NIHSS 14, mean age 63 years) were treated with intracranial stents for acute ischemic stroke. Occlusions were located in the posterior vertebrobasilar circulation (n = 6) and in the anterior circulation (n = 6). Stent placement was feasible in all procedures and resulted in partial or complete recanalization (TIMI 2/3) in 92%. No vessel perforations, subarachnoid, or symptomatic intracerebral hemorrhages occurred. One dissection was found after thromboaspiration and PTA. Three patients (25%) had a good outcome (mRS 0 to 2), 3 (25%) a moderate outcome (mRS 3), and 6 (50%) a poor outcome (mRS 4 to 6). Mortality was 33.3%.

Conclusions—Intracranial placement of a self-expandable stent for acute ischemic stroke is feasible and seems to be safe to achieve sufficient recanalization. (Stroke. 2009;40:847-852.)

Key Words: ischemic stroke ■ interventional neuroradiology ■ stent ■ endovascular therapy

Successful recanalization is associated with improved outcome after acute ischemic stroke.1 Mechanical thromboembolectomy (MT) techniques are proposed for treatment in case of failed recanalization after thrombolysis or in patients with contraindications for thrombolytic therapy. However, mechanical recanalization techniques are not always successful. For instance, the FDA approved Merci Retriever System failed to achieve recanalization in a large proportion of patients (43% to 54%) treated up to 8 hours after symptom onset.2,3

Stents have been used to recanalize occluded or severely stenosed cervical arteries to increase blood flow to the cerebral arteries in acute stroke patients.4–6 With the advent of small sized cardiological stents some investigators used these balloon-mounted stents for recanalization of acute occluded cerebral arteries.7–10 Levy et al were the first reporting the use of self-expandable stents in the setting of acute ischemic stroke,11 Recanalization rates of 79% to 90% have been reported so far, mostly for vessel occlusions resistant to other therapies.7,10,11 However, sample sizes were small and various types of stents, as well as manifold combinations with percutaneous balloon angioplasty (PTA), Merci-retrieval, mechanical disruption, intravenous, or intraarterial thrombolysis (IAT) were used. Moreover, symptomatic intracranial hemorrhages (sICH) or subarachnoid hemorrhages (SAH) occurred in 14% to 50% of treated patients and are supposed to be at least partially related to the balloon-mounted stent technique.9,10

Our group implemented stenting as an additional treatment option for intracranial recanalization in stroke patients after assessing PTA and stent placement in acute embolic occlusions in the Bernese stroke animal model.12 This study evaluates the intracranial placement of a self-expandable stent as a rescue procedure for acute ischemic stroke with special regard to feasibility, recanalization rate, complications, and outcome.

Methods
All patients treated at our department with intracranial stent placement for acute cerebral artery occlusion were retrospectively ana-
lyzed. Data had been collected prospectively and entered into our stroke database. Inclusion criteria for intracranial stent treatment were confirmed vessel occlusion by digital subtraction angiography (DSA), failed IAT, or contraindication to perform intravenous thrombolysis (IVT) or IAT (eg, previous cerebral infarct, surgery, or warfarin therapy). Inclusion criteria for IAT were (1) clinical diagnosis of acute stroke established by a stroke neurologist; (2) baseline NIHSS score >4, except for isolated aphasia or hemianopia; (3) exclusion of hemorrhage by cranial Computed Tomography (CT) or Magnetic Resonance Imaging (MRI); (4) vessel occlusion correlating to neurological deficit confirmed by 4- vessel angiography; (5) initiation of treatment within 6 hours of symptom onset for hemispheric stroke and within 12 hours for vertebrobasilar stroke; (6) no clinical or laboratory contraindications for IAT; (7) for patients >75 years that their general condition before stroke did not advise against it; (8) informed consent of the patient or next of kin.16 Baseline investigations included a neurological and physical examination, assessment of stroke severity using the National Institutes of Health Stroke Scale (NIHSS), routine blood analysis, and 12-lead ECG.

**Arteriography**

Interventions were performed in the neuroangiography laboratory equipped with a biplane, high-resolution angiography system (CAS 500, Toshiba). Except for one patient who had local anesthesia, all stents were deployed under general anesthesia. After placement of a 7- to 8-Fr catheter sheath in the common femoral artery a 4-vessel DSA including all cerebral arteries was performed to assess the site of vessel occlusion and collateral circulation. Collateral flow was graded regarding to the grading system proposed by the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology: Grade 0, no collaterals visible to the ischemic site; grade 1, slow collaterals to the periphery of the ischemic site with persistence of some of the defect; grade 2, rapid collaterals to the periphery of the ischemic site with persistence of some of the defect and to only a portion of the ischemic territory; grade 3, collaterals with slow but complete angiographic blood flow to the ischemic bed occurring by the late venous phase; grade 4, except for isolated aphasia or hemianopia; grade 3, complete revascularization.17 Thrombus formation or residual thrombus inside the stent lumen as well as side wall irregularities corresponding to residual atherosclerotic stenosis or fixed thrombotic material between stent and vessel wall were recorded. Dissection and vessel perforation were assessed. Flow in the lenticulostriate arteries (LA) after stent placement in the middle cerebral artery (MCA) was evaluated and perfusion of major branches (eg, M2 segments, cerebellar arteries, posterior cerebral artery) after revascularization of the main vessel was assessed.

**Patient Care and Follow-Up**

After the intervention patients were transferred to the intensive care unit. Brain CT or MRI was performed in the first 24 hours after intervention as well as in case of neurological deterioration to exclude intracranial hemorrhage and to estimate brain edema. sICH was defined as clinical deterioration (4-point or greater increase in the NIHSS score or a 1-point deterioration in the level of consciousness) combined with space-occupying brain hematoma.15,18 After exclusion of hemorrhage, long-term aspirin (100 mg/d) was given and clopidogrel (75 mg/d) was added for the next 30 days. Clinical outcome was assessed at 3 months according to the modified Rankin scale (mRS).19 Outcome was stratified to “good outcome” (mRS 0 to 2), “moderate outcome” (mRS 3), and “poor outcome” (mRS 4 to 6).

Stent patency at follow-up was assessed by transcranial ultrasound (n = 8), MR-Angiography (n = 6), and CT-Angiography (n = 4) in the first 72 hours after stent placement. Two patients died before follow-up examination of vessel patency.

**Results**

From May 2006 until July 2007, 77 patients were treated by endovascular means for acute ischemic stroke at our department. Twelve patients (7 men and 5 women, mean age 63 ± 13 years) suffering acute cerebral artery occlusion were treated by intracranial stent placement and are included in this study. Indication for stent placement was failed IAT or MT (n = 7), previous surgery, warfarin therapy, progressive stroke with preexisting brain infarct, vessel occlusion during aneurysm coiling after acute SAH, and recanalization of the intradural VA to allow IAT for thrombosis of the basilar artery (BA; n = 1 each). Median NIHSS score at admission was 14 (range 5 to 38). Either CT (n = 4) or MRI (n = 8) was performed before treatment was initiated.

In 11 patients 1 stent was deployed, and in 1 patient 3 stents were delivered. Stent placement was feasible in all 14 stent procedures. Occlusion sites are given in the Table. All patients had collateral flow grade 2. We made the decision to place a stent in 4 patients in whom PTA had been unsuccessful. PTA was performed in a further 4 patients before and in 3 patients after stent placement. Partial or complete recanalization (TIMI 2 and 3) was achieved in 11/12 patients (91.6%). Median time from symptom onset to recanalization was 393 minutes (range 20 to 510 minutes.).

One dissection of a VA was visible after aspiration and PTA. No vessel perforations or dissections related to the stent placement were noted, and no SAH or sICH was detected by follow-up CT or MRI. Vessel wall irregularities were found immediately after stent placement in all patients (Figure 1).
Preservation of LA was possible in all stent placements in the middle cerebral artery (MCA). Occlusion of a major vessel branch at the site of stent placement persisted in 6 patients. Assessment of the dependent vessel branch territory by follow-up MRI or CT showed infarction in 3 of 6 patients (50%), whereas no infarction of this particular territory was noted in the remaining 3 patients. In 8 patients major branches at the site of the stent showed sufficient perfusion (Figure 1).

Thrombus formation inside the stent was found in 1 patient. It started during coil embolization of an anterior communicating artery aneurysm and continued after a stent had been deployed to recanalize the acutely occluded A1 segment. Subsequent intraarterial application of a glycoprotein IIb/IIIa receptor inhibitor (ReoPro 20 mg, Lilly) resulted in regression of luminal clot. In a further case repeated passages with the aspiration catheter and microcatheter to recanalize the BA caused a dislocation of the proximal stent markers without effect on revascularization result (Figure 2).

At 3 months follow-up 3 patients (25%) had a good outcome (mRS 0 or 1), 3 (25%) had a moderate outcome (mRS 3), and 6 (50%) had a poor outcome (mRS 4 to 6). Mortality was 33.3%.

Discussion

A recent meta-analysis of several stroke studies revealed a strong association of recanalization and good outcome after acute ischemic stroke.1 IVT has been shown to improve patient outcome and is approved by the FDA and EMEA.20 However, only a minority of patients admitted for acute stroke receive IVT.21 IAT is also effective for vessel recanalization and is supposed to achieve higher recanalization rates than IVT.13,18 On the other hand, application of thrombolytic drugs increases the risk of sICH.6,15,20 These

Table.

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NA indicates not assessable; ACA, anterior cerebral artery; M1, middle cerebral artery main stem; BA, basilar artery; CTO, carotid-T-occlusion; PCA, posterior cerebral artery; VA, vertebral artery; IAT, intraarterial thrombolysis; UK, urokinase; MT, mechanical thromboembolectomy; PTA, percutaneous transluminal balloon angioplasty; †Before and after stent placement; †time from stroke onset to treatment, resp. recanalization in minutes; ‡modified Rankin scale score at 3 months follow-up.

Figure 1. 81-year-old patient presenting with acute right-sided hemiplegia and aphasia (NIHSS 18). Diffusion-weighted MR image at the level of the basal ganglia (a) depicted acute infarction in the territory of the lenticulostriate arteries (LA). Left carotid angiogram confirmed occlusion (arrow, b) of the left middle cerebral artery (MCA, M1 segment). Unsubtracted image of anterior-posterior (AP) projection documented the position of the tip of the microcatheter (c). The thrombus had been passed at the side of the LA (arrow, c). After local application of Urokinase minimal recanalization was achieved (d), considered as hemodynamically insufficient. Therefore the thrombus was passed with a long exchange microwire placed in the superior branch of the left MCA. Consequently a stent was deployed at the occlusion site, and flow was immediately restored (e). Flow into LA through the stent mesh (white arrow) was achieved. Residual thrombus remained at the origin of the inferior branch (black arrow head). Follow-up MRI performed 2 days later revealed a small embolic infarction (arrow, f) in the left MCA territory but no significant increase of infarcted tissue.
Factors as well as failure of thrombolysis to achieve sufficient recanalization in a subgroup of patients led to the introduction of MT. The Merci Retriever System got FDA approval in 2004. However, recanalization rate remained at 46% to 57% with the Merci retriever and risk of SAH attributable to intracranial vessel perforation has increased.

No technical failure was encountered in our study. The stent catheter was navigated easily up to the intracranial vasculature and placed beyond the occlusion site. High recanalization rates of 79% to 90% after intracranial stent placement have been reported and are confirmed in the present study (92%). Whereas Levy et al reported results obtained at 4 different clinical centers and used the Neuroform stent in a majority of patients, we report a single center experience with the more recently introduced Wingspan stent system. Compared to the Neuroform stent the Wingspan stent has an improved delivery system, a higher radial force, and a higher number of struts. The improved delivery system increases stent safety and feasibility. The higher radial force and tighter struts are supposed to compress and fixate the thrombus more reliably.

Mortality (33%) was similar to former studies (32% to 40%), and a good outcome after 3 months was observed only in a quarter of the patients. However, stenting was performed as a rescue therapy in patients with major artery occlusions after failure of other techniques. This resulted in a median time from symptom onset to recanalization of 393 minutes and might explain the poor clinical outcome. Additionally, half of our patients suffered of BA occlusion, which is known to be associated with a high rate of poor clinical outcome. Three of 4 deaths in our study are in that group and were caused by aspiration pneumonia. The fourth deceased patient had a carotid-T-occlusion, which is also known to respond poorly to recanalization and often has a poor prognosis. The latter case represents the only insufficient recanalization in our study: stent deployment had been uneventful in this patient, but blood flow to the dependent brain parenchyma was obviously reduced resulting in early reocclusion. The patient died 2 days later because of increasing brain edema.

In accordance with the results of a previous study no dissection or vessel perforation was recorded attributable to stent placement itself. One dissection of a VA was noticed before stent placement related to repeated thromboaspiration maneuvers and PTA. Remarkably, occurrence of sICH and SAH in our patients was significantly lower than reported (none versus 14% to 50%). One explanation might be the use of a self-expandable stent compared to balloon-mounted stents investigated in prior studies. Balloon-mounted stents developed for cardiology are less flexible than self-expandable stents. Therefore, their application causes more mechanical stress to the vessel wall during the navigation into the relatively small intracranial arteries. Additionally, the necessity for stiffer microwires that have to be placed in the periphery of the cerebral arteries increases the risk of perforation, eg, all 4 patients treated with a balloon-mounted stent in the study of Sauvageau et al suffered SAH. Moreover, self-expandable stents apply a lower radial force than the inflation of balloon-mounted stents, reducing the risk of vessel rupture in case of hard thrombus or atherosclerotic stenosis. After deployment the self-expanding force persists and might improve recanalization result with time as thrombus gets resorbed. Besides the mechanical aspects of the applied stent, concomitant antiplatelet therapy in combination with thrombolysis might have increased bleeding rates in previous studies: whereas Levy et al applied glycoprotein IIb/IIIa receptor inhibitors in addition to aspirin, clopidogrel, heparin, and thrombolitics, a glycoprotein IIb/IIIa receptor inhibitor was given only in one of our patients who had not received thrombolysis. Additionally, heparin was not used in our patients aside from catheter flushing. The combination of UK, aspirin, and clopidogrel did not cause sICH in our small patient group.

However, local platelet activation attributable to thrombus, vessel wall injury, and the stent itself remains a major concern. Immediate application of aspirin after stent placement followed by a combination therapy of aspirin and clopidogrel for the next 4 weeks after exclusion of hemorrhage seems efficient to avert stent occlusion. Keeping in mind the higher bleeding rates reported in studies using a combination of aspirin, clopidogrel, glycoprotein IIb/IIIa receptor inhibitor, and thrombolitics, as well as the
unfavorable results of the Abciximab in Emergency Treatment of Stroke Trial (AbESTT),26 we advocate the use of glycoprotein IIb/IIIa receptor inhibitors only in case of acute thrombus formation after stent placement. Using this regimen, we have observed no recurrences or embolic events caused by the stent during follow-up.

From our point of view important side branches like the LA can be preserved if the thrombus is passed on the ipsilateral side by the microwire and the stent. Stent expansion will fixate the thrombus at the contralateral wall. This technique was successfully performed in all 5 of our patients suffering MCA occlusion and can be translated to the BA and P1 segments with their perforating arteries as well. However, occlusion of major vessel branches (eg, M2 segment, superior cerebellar artery) at the site of stent placement persisted in 6 patients. Remarkably, no infarction occurred in the dependent vessel territory in half of those patients, pointing to a sufficient collateral circulation. In 3 patients follow-up MRI or CT revealed infarcts in the dependent vessel territory. These infarcts were apparent to some extent at MRI before the interventional treatment, and it remains uncertain whether they are related to the primary occlusive disease or to the stent placement.

In our experience care has to be taken if the deployed stent has to be passed repeatedly with other devices. As long as the stent is not covered by neointima, devices might get caught in the stent struts with subsequent complications (ie, stent dislocation or deformation [Figure 2], device rupture, or failure to remove the device). Hence stent placement was performed to reestablish sufficient cerebral blood flow with as little mechanical manipulation as possible, additional postdilatation was performed in only 25% of our patients.

Before the introduction of stents for the treatment of atherosclerotic stenosis of intracranial vessels, PTA performed alone for acute ischemic stroke yielded some success.27–29 However, when treating thrombus rather than atherosclerotic stenosis, recollision attributable to thrombogenesis and thrombus expansion might occur.7 In our study all PTAs performed for vessel recanalization failed to establish sufficient flow.

Limitations
Because of the retrospective nature of the study, the inhomogeneous and small patient collective, and the different therapies used in addition to the placement of an intracranial stent, results have to be interpreted with caution.

Summary
This study illustrates the feasibility of intracranial stent placement for acute stroke treatment. Recanalization rate was high, and the rate of major complications was low. However, clinical outcome, at least partially influenced by patient selection, was poor. Further controlled randomized trials to prove its safety and efficacy in a larger number of patients are needed.

Disclosures
None.

References
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